

U.S.S.N. 09/978,333

Filed: October 15, 2001

**AMENDMENT AND RESPONSE TO OFFICE ACTION****Amendment****In the Claims**

1-6. (canceled)

7. (previously presented) A method for targeted recombination of a nucleic acid molecule comprising the steps of:

a) providing a single-stranded oligonucleotide having a sequence that forms a triple-stranded nucleic acid molecule by hybridizing with a target sequence in a double-stranded nucleic acid molecule with a  $K_d$  of less than or equal to  $2 \times 10^{-7}$ ; and

b) providing a donor nucleic acid such that recombination of the donor nucleic acid into the target sequence is induced by triple helix formation between the single-stranded oligonucleotide and the double-stranded nucleic acid molecule.

8. (previously presented) The method of claim 7, wherein the single-stranded oligonucleotide is between 10 and 60 nucleotides in length.

9. (previously presented) The method of claim 7, wherein the single-stranded oligonucleotide is tethered to the donor nucleic acid.

10. (previously presented) The method of claim 7 wherein the double-stranded nucleic acid molecule encodes a protein and the targeted recombination of the donor nucleic acid with the double-stranded nucleic acid molecule alters the activity of the protein encoded by the double-stranded nucleic acid molecule.

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11. (original) The method of claim 7, wherein the double-stranded nucleic acid molecule is selected from the group consisting of a gene, an oncogene, a defective gene, a viral genome, and a portion of a viral genome.

12. (previously presented) The method of claim 7, wherein the donor nucleic acid is at least 30 nucleotide residues in length.

13-14. (canceled)

15. (currently amended) The method of claim 7 to produce changes in the genome of an intact human or animal ~~further comprising the steps of: wherein~~

~~administering~~ the single-stranded oligonucleotide is administered into an intact human or animal having a sequence that forms a triple-stranded nucleic acid molecule with the target sequence located in the genome of the intact human or animal, wherein the oligonucleotide binds to the target sequence with a  $K_d$  of less than or equal to  $2 \times 10^{-7}$ , and mutates the target sequence.

16. (original) The method of claim 15 wherein the oligonucleotide is between 10 and 60 nucleotides in length.

17. (original) The method of claim 15 wherein the oligonucleotide is dissolved in a physiologically acceptable carrier.

18. (original) The method of claim 15 wherein the oligonucleotide is recombinagenic.

19. (previously presented) The method of claim 18 wherein the oligonucleotide stimulates recombination of an exogenously supplied donor nucleic acid with the target sequence of the genome.

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20. (previously presented) The method of claim 18 wherein the oligonucleotide stimulates recombination of a donor nucleic acid that is tethered to the oligonucleotide with the target sequence of the genome.

21. (previously presented) The method of claim 15 wherein the target sequence is selected from the group consisting of a gene, an oncogene, a defective gene, a viral genome, and a portion of a viral genome.

22. (previously presented) The method of claim 21 wherein the gene is a defective - hemoglobin gene, cystic fibrosis gene, xeroderma pigmentosum gene, nucleotide excision repair pathway gene, or hemophilia gene.

23. (original) The method of claim 15 wherein the oligonucleotide is composed of homopurine or homopyrimidine nucleotides.

24. (previously presented) The method of claim 15 wherein the oligonucleotide is composed of polypurine or polypyrimidine nucleotides.

25. (previously presented) The method of claim 9 wherein the donor nucleic acid is between 10 and 40 nucleotides.